

## Abstract

### THE ACTIVITY OF MATRIX METALLOPROTEINASE-2 AND TISSUE INHIBITORS OF METALLOPROTEINASE-2 ARE ASSOCIATED WITH THE DEGREE OF ENDOMETRIOMA TISSUE INVASION TRANSPLANTED ONTO THE CHORIOALLANTOIC MEMBRANE (CAM)

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**Background.** Endometrioma are cystic lesion which arises from endometriosis process. Endometrioma are commonly found in the ovary. The early developmental process of endometrioma formation is started when endometrial tissue attached and grew on ovarian epithelium. Progressive invagination of the ovarian cortex on to these attached tissue might lead to the formation of an endometrioma. Other study hypothesized that in endometrioma formation, the viable endometrial cells spread via hematogenous or lymphatic to develop metaplasia and differentiation into endometrial cells. One of the fundamental pathogenesis of endometriosis to grow and develop is to carry out cellular invasion of the surrounding tissue where it attaches. The invasion process of endometriotic focus is linked with the activity of matrix metalloproteinases-2 (MMP-2) and tissue inhibitors of metalloproteinases-2 (TIMP-2). In this study, we used endometrioma tissue to be implanted in chick chorioallantoic membrane (CAM) as a culture medium to reconstruct the invasion process of endometriosis, and then the MMP-2, TIMP-2 and invasion pattern can be invitro observed.

**Materials and methods.** This study was an observational laboratory study. The objective is to observe activity of MMP-2, TIMP-2 expression in different level invasion of endometrioma tissue transplanted onto CAM. Endometrioma tissue fragments taken from patients with ovarian endometrioma by laparoscopic surgery. The tissue fragments were divided into 4-8 strips with dimension each of 2 x 2 mm. Two strips were assessed for the activity of MMP-2. Two remaining strips were transplanted onto the CAM. After incubation for five days, the transplanted tissues were harvested for assessment of MMP-2, TIMP-2 and histological assessment. Histological assessment for the invasion level was carried out by hematoxylin-eosin staining, the assessment of MMP-2 by gelatin zymography and TIMP-2 by western blot. The invasion level number 1 is for non invasion, level 2 for partial invasion < 50%, level 3 for partial invasion > 50%, and level 4 for total invasion.

**Result.** Twenty four fragments of endometrioma have been collected from 24 endometrioma patients who underwent laparoscopy surgery. The average age was  $31 \pm 5$  years, BMI was  $22 \pm 3$  kg/m<sup>2</sup>, duration of infertility was  $58 \pm 3$  month and r-ASRM was  $67 \pm 36$ . In CAM of transplanted endometriomas tissue, MMP-2 activity was positively correlated with TIMP-2 with moderate relationship ( $r_t = 0,56$ , p-value < 0,05), weak positive correlation with invasion score ( $r_t = 0,08$ , p-value > 0,05). TIMP-2 expression was negatively correlated with invasion score

with strong relationship ( $r_t = -0,35$ , p-value  $< 0,05$ . Ratio between MMP-2/TIMP-2 was positively correlated with invasion score with very strong relationship ( $r_t = 0,72$ , p-value  $< 0,05$ )

**Conclusion.** The ratio of MMP-2/TIMP-2 had a positive relationship, MMP-2 had a positive relationship and TIMP-2 had a negative relationship with the level of endometrioma invasion transplanted onto CAM

**Keywords:** Endometrioma, MMP-2, TIMP-2, invasion, CAM